



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Oldfield et al.

Application No. 10/528,310

Filed: March 17, 2005

Confirmation No. 7600

For: METHOD FOR CONVECTION
ENHANCED DELIVERY OF
THERAPEUTIC AGENTS

Examiner: Karen Carlson

Art Unit: 1653

Attorney Reference No. 4239-66640-05

CERTIFICATE OF MAILING

I hereby certify that this paper and the documents referred to as being attached or enclosed herewith are being deposited with the United States Postal Service as First Class Mail in an envelope addressed to: COMMISSIONER FOR PATENTS, P.O. BOX 1450, ALEXANDRIA, VA 22313-1450 on the date shown below.

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Date Mailed

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DECLARATION OF DR. EDWARD OLDFIELD UNDER 37 C.F.R. §1.132

I, Dr. Edward Oldfield, hereby declare as follows:

I am a co-inventor of the subject matter described and claimed in the patent application referenced above, i.e., U.S. Patent App. No. 10/528,310 (hereafter the "310 application").

I understand that several claims pending in the '310 application have been rejected in view of the disclosure in Laske, Youle, Oldfield, Tumor regression with regional distribution of the targeted toxin TF-CRM107 in patients with malignant brain tumors, *Nature Medicine* 3:1362-1368 (December 1997) (hereafter the "Laske et al. article").

The Office action on page 3 states that "it appears that Laske et al. used a tracer (Gd; claims 5,30) with the therapeutic agent Tf-CRM107 to monitor the distribution of the solution in the brain (claims 25,27) by imaging via MRI (claim 4) the tracer (claim 1), and ceased the delivery when the volume reached 40ml (claim 2,26) at the target tissue (claim 3). In support of this position, the Office action cites Table 2, footnote 1, of the Laske et al. article which states

that "Tf-CRM107 concentration was initially kept constant at 0.1 µg/ml while the volume was escalated to 40 ml to improve drug distribution as assessed by MRI (volume of necrosis and infusion edema)."

I am a co-author of the Laske et al. article. My recollection is that in the studies reported in the Laske et al. article MRI was performed after infusion of Tf-CRM107 rather than during infusion. The MRI was performed to assess tumor growth (see page 1368, column 1, of Laske et al. – "After evaluating the volume of tumor necrosis and infusion edema generated in patients 1 and 2 in the initial MRIs, it was evident that larger infusion volumes were required to perfuse the tumor margins"). In addition, there was no infusion of a solution that contained both Tf-CRM107 and Gd.

All statements made herein and of my own knowledge are true and all statements made on information are believed to be true; and further, these statements were made with the knowledge that willful false statements and the like are punishable by fine and imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Date: October 18, 2007

Edward H. Oldfield
Name: Dr. Edward Oldfield